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June 11, 2004 — Date

Gina N. Shishima

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Murphy et al.

Serial No.: 10/029,397

Filed: December 20, 2001

For: METHOD AND SYSTEM FOR DEPLETING rRNA POPULATIONS

Group Art Unit: 1634

Examiner: Whisenant, Ethan C.

Atty. Dkt. No.: AMBI:076US

I. AMENDMENT; AND II. RESPONSE TO OFFICE ACTION DATED MARCH 11, 2004

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

This paper is submitted in response to the Office Action dated March 11, 2004 for which the three-month date for response is June 11, 2004.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski L.L.P. Account No.: 50-1212/AMBI:076US.

Reconsideration of the application is respectfully requested.

I. AMENDMENT

Please amend the claims as follows:

1. (Currently Amended) A method for depleting ~~or isolating~~ a targeted nucleic acid from a sample comprising:

a) incubating the sample with a first bridging oligonucleotide comprising (1) at least one bridging region comprising at least 5 nucleic acid residues and (2) at least one targeting region comprising at least 5 nucleic acid residues, under conditions allowing hybridization between the first targeting region and the targeted nucleic acid;

b) incubating the first bridging oligonucleotide with a capture oligonucleotide comprising a nonreacting structure and a capture region comprising at least 5 nucleic acid residues, under conditions allowing hybridization between the bridging region and the capture region; ~~and~~

c) isolating the targeted nucleic acid from the remainder of the sample, wherein the targeted nucleic acid is depleted from the sample; and,

d) utilizing nontargeted nucleic acids in the depleted sample ~~discarding the targeted nucleic acid~~.

2. (Original) The method of claim 1 wherein the targeted nucleic acid is rRNA.

3. (Original) The method of claim 2, wherein the rRNA is prokaryotic 16S, prokaryotic 23S, eukaryotic 17S or 18S, or eukaryotic 28S rRNA.

4. (Original) The method of claim 3, wherein the rRNA comprises the sequence of SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID

NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:72, or SEQ ID NO:73.

5. (Original) The method of claim 1, wherein the sample comprises eukaryotic nucleic acid.

6. (Original) The method of claim 1, wherein the sample comprises prokaryotic nucleic acid.

7. (Original) The method of claim 6, wherein the prokaryotic nucleic acid is from a gram positive bacterium.

8. (Original) The method of claim 6, wherein the prokaryotic nucleic acid is from a gram negative bacterium.

9. (Original) The method of claim 1, wherein the bridging region, targeting region, or capture region comprises at least 10 nucleic acid residues.

10. (Original) The method of claim 9, wherein the bridging region, targeting region, or capture region comprises at least 15 nucleic acid residues.

11. (Original) The method of claim 10, wherein the bridging region, targeting region, or capture region comprises at least 20 nucleic acid residues.

12. (Original) The method of claim 1, wherein the bridging region or the capture region is polypurine or polypyrimidine.

13. (Original) The method of claim 12, wherein the bridging region is polypurine and the capture region is polypyrimidine.

14. (Original) The method of claim 1, further comprising incubating the sample with a second bridging oligonucleotide comprising (1) at least one bridging region comprising at least 5 nucleic acid residues and (2) at least one targeting region comprising at least 5 nucleic acid residues, under conditions allowing hybridization between the targeting region of the second bridging oligonucleotide and the targeted nucleic acid.

15. (Original) The method of claim 14, wherein the targeting region of the first bridging oligonucleotide is complementary to the sequence of a targeted nucleic acid and the targeting region of the second bridging oligonucleotide is complementary to a different sequence of a targeted nucleic acid.

16. (Original) The method of claim 15, wherein the targeting region of the first bridging oligonucleotide and the targeting region of the second bridging oligonucleotide are complementary to the same targeted nucleic acid.

17. (Original) The method of claim 15, wherein the targeting region of the first bridging oligonucleotide and the targeting region of the second bridging oligonucleotide are complementary to different targeted nucleic acids.

18. (Original) The method of claim 17, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of the largest rRNA molecule and the targeting region of the second bridging oligonucleotide is complementary to a sequence of the second largest rRNA molecule in the sample.

19. (Original) The method of claim 14, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 100 and 5000 residues of the 5' or 3' end of the targeted nucleic acid.

20. (Original) The method of claim 19, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 150 and 4000 residues of the 5' or 3' end of the targeted nucleic acid.

21. (Original) The method of claim 20, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 200 and 3000 residues of the 5' or 3' end of the targeted nucleic acid.

22. (Original) The method of claim 21, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 250 and 2000 residues of the 5' or 3' end of the targeted nucleic acid.

23. (Original) The method of claim 22, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 300 and 1500 residues of the 5' or 3' end of the targeted nucleic acid.

24. (Original) The method of claim 23, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 350 and 1000 residues of the 5' or 3' end of the targeted nucleic acid.

25. (Original) The method of claim 24, wherein targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 400 and 900 residues of the 5' or 3' end of the targeted nucleic acid.

26. (Original) The method of claim 25, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 450 and 800 residues of the 5' or 3' end of the targeted nucleic acid.

27. (Original) The method of claim 26, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 500 and 700 residues of the 5' or 3' end of the targeted nucleic acid.

28. (Original) The method of claim 14, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence at the 3' or 5' end of the targeted nucleic acid.

29. (Original) The method of claim 14, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence not within 100 residues from the 3'or 5' end of the targeted nucleic acid.

30. (Original) The method of claim 14, wherein targeting region of the first or second bridging oligonucleotide hybridizes to a sequence not within 200 residues from the 3'or 5' end of the targeted nucleic acid.

31. (Original) The method of claim 14, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence not within 400 residues from the 3'or 5' ends of the targeted nucleic acid.

32. (Original) The method of claim 14, wherein the targeting region of the first or second bridging oligonucleotide comprises SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, or SEQ ID NO:22.

33. (Original) The method of claim 1, wherein the bridging oligonucleotide comprises a second targeting region comprising at least 5 nucleic acid residues complementary to a different sequence than the sequence to which the first targeting region is complementary.

34. (Currently amended) The method of claim 33, wherein the first targeting region is complementary to a different targeted [targeting] nucleic acid than the second targeting region is.

35. (Original) The method of claim 1, wherein the first bridging oligonucleotide comprises two bridging regions.

36. (Original) The method of claim 1, wherein the bridging oligonucleotide or the capture oligonucleotide is RNA, DNA, LNA, iso-bases, or a peptide nucleic acid.

37. (Original) The method of claim 1, further comprising washing the capture oligonucleotide after incubation with the sample and the bridging oligonucleotide.

38. (Original) The method of claim 1, wherein a) and b) are performed at the same temperature.

39. (Original) The method of claim 1, wherein a) and b) are performed at a different temperature.

40. (Original) The method of claim 38, wherein a) and b) are performed at the same time.

41. (currently amended) The method of claim 1, wherein the nonreacting structure comprises a bead comprising plastic, glass, teflon, silica, a magnet, ~~cellulose,~~ latex, polystyrene, nylon, cellulose, nitrocellulose, polymethacrylate, polyvinylchloride, or styrene-divinylbenzene

42. (Original) The method of claim 41, wherein isolating the targeted nucleic acid away from the sample comprises exposing the sample with the capture oligonucleotide to a magnetic field.

43. (Original) The method of claim 1, wherein the nonreacting structure is cellulose.

44. (Original) The method of claim 1, wherein the nonreacting structure is biotin.

45. (Original) The method of claim 44, wherein isolating the targeted nucleic acid comprises incubating the sample with streptavidin or avidin.

46. (Original) The method of claim 1, wherein the sample, capture oligonucleotide, and bridging oligonucleotide are incubated in a buffer comprising TMAC or TEAC.

47. (Cancelled)

48. (Previously presented) The method of claim 2, further comprising:

d) ~~discarding the targeted rRNA nucleic acid; and~~

~~e)~~ producing cDNA using mRNA in the remainder of the sample.

49. (Original) The method of claim 48, further comprising:

f) attaching the cDNA to a solid support, wherein a nucleic acid array is created.

50. (Original) The method of claim 49, wherein the solid support is plastic, glass, or nylon.

51. (Original) The method of claim 50, wherein the solid support is a plate.

52. (Original) The method of claim 51, wherein the plate is a multiple-well plate.

53. (Original) The method of claim 48, further comprising:

f) contacting a nucleic acid array with the cDNA.

54. (Previously presented) A method for depleting rRNA from a sample comprising:

a) incubating the sample with at least a first (1) bridging oligonucleotide comprising a bridging region comprising a poly-purine region of at least 5 residues and a targeting region comprising at least 5 contiguous nucleic acid residues complementary to a sequence of an rRNA molecule and a (2) capture oligonucleotide comprising a magnetic bead and a capture region comprising a

poly-pyrimidine region of at least 5 residues, under conditions to allow hybridization between the bridging oligonucleotide and the capture oligonucleotide and the bridging oligonucleotide and the rRNA;

b) incubating the sample with a magnetic bead; ~~and~~

c) isolating the magnetic bead; and,

d) discarding the magnetic bead with the rRNA.

55. (Withdrawn) A kit, in a suitable container means, comprising:

a) a capture oligonucleotide comprising a capture region and a magnetic bead; and

b) at least a first bridging oligonucleotide comprising (1) at least one bridging region complementary to all or part of the capture region of the capture oligonucleotide and a (2) at least one targeting region comprising 10 contiguous nucleic acids complementary to a sequence of an rRNA.

56. (Withdrawn) The kit of claim 55, wherein the first bridging oligonucleotide comprises a second targeting region.

57. (Withdrawn) The kit of claim 56, wherein the first and second targeting regions have the same nucleic acid sequence.

58. (Withdrawn) The kit of claim 56, wherein the first and second targeting regions have different nucleic acid sequences.

59. (Withdrawn) The kit of claim 58, wherein the first targeting region is complementary to a sequence of an eukaryotic rRNA and the second targeting region is complementary to a sequence of a prokaryotic rRNA.

60. (Withdrawn) The kit of claim 58, wherein the first targeting region is complementary to a sequence of an eukaryotic rRNA and the second targeting region is complementary to a sequence of a different eukaryotic rRNA than the first targeting region.

61. (Withdrawn) The kit of claim 58, wherein the first targeting region is complementary to a sequence of a prokaryotic rRNA and the second targeting region is complementary to a sequence of a different prokaryotic rRNA than the first targeting region.

62. (Withdrawn) The kit of claim 55, further comprising a second bridging oligonucleotide comprising (1) at least one bridging region complementary to all or part of the capture region of the capture oligonucleotide and a (2) at least one targeting region comprising 10 contiguous nucleic acids complementary to a sequence of an rRNA.

63. (Withdrawn) The kit of claim 62, wherein the targeting region of the second bridging oligonucleotide is complementary to a sequence of the same rRNA as the first targeting region.

64. (Withdrawn) The kit of claim 62, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of the largest rRNA and the targeting region of the second bridging oligonucleotide is complementary to a sequence of the second largest rRNA in the sample.

65. (Withdrawn) The kit of claim 62, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of an eukaryotic rRNA and the targeting region of the bridging oligonucleotide is complementary to a sequence of a prokaryotic rRNA.

66. (Withdrawn) The kit of claim 64, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of an eukaryotic 28S rRNA and the targeting region of the second bridging oligonucleotide is complementary to a sequence of a eukaryotic 17S or 18S rRNA.

67. (Withdrawn) The kit of claim 64, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of a prokaryotic 23S rRNA and the targeting region of the second bridging oligonucleotide is complementary to a sequence of a prokaryotic 16S rRNA.

68. (Withdrawn) The kit of claim 64, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of an eukaryotic 28S rRNA and the targeting region of the second bridging oligonucleotide is complementary to a sequence of a prokaryotic 23S rRNA.

69. (Withdrawn) The kit of claim 62, further comprising a third bridging oligonucleotide comprising (1) at least one bridging region complementary to all or part of the capture region of the capture oligonucleotide and a (2) at least one targeting region comprising 10 contiguous nucleic acids complementary to a sequence of an rRNA.

70. (Withdrawn) The kit of claim 69, wherein the targeting region of the third bridging oligonucleotide is complementary to a sequence of a prokaryotic 23S rRNA.

71. (Withdrawn) The kit of claim 69, wherein the targeting region of the third bridging oligonucleotide is complementary to a sequence of a eukaryotic 18S rRNA.

72. (Withdrawn) The kit of claim 69, further comprising a fourth bridging oligonucleotide comprising (1) at least one bridging region complementary to all or part of the capture region of the capture oligonucleotide and a (2) at least one targeting region comprising 10 contiguous nucleic acids complementary to a sequence of an rRNA.

73. (Withdrawn) The kit of claim 72, wherein (i) the targeting region of the first bridging oligonucleotide is complementary to a sequence of a prokaryotic 16S rRNA, (ii) the targeting region of the second bridging oligonucleotide is complementary to a sequence of a prokaryotic 23S rRNA, (iii) the targeting region of the third bridging oligonucleotide is complementary to a sequence of a eukaryotic 18S rRNA, and (iv) the targeting region of the fourth bridging oligonucleotide is complementary to a sequence of a eukaryotic 28S rRNA,

74. (Withdrawn) The kit of claim 55, wherein the first targeting region of the bridging oligonucleotide comprises SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID

NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, or SEQ ID NO:22.

75. (Withdrawn) The kit of claim 55, further comprising a buffer comprising TMAC or TEAC.

76. (Withdrawn) The kit of claim 55, further comprising a magnetic stand.

77. (Withdrawn) The kit of claim 55, further comprising:

c) a solid support for preparing a nucleic acid array.

78. (Withdrawn) A bridging oligonucleotide comprising a (1) bridging region comprising a polypyrimidine or polypurine stretch and a (2) targeting region comprising at least 10 contiguous nucleic acid residues complementary to a sequence of an rRNA.

79. (Withdrawn) The oligonucleotide of claim 78, wherein the rRNA is eukaryotic.

80. (Withdrawn) The oligonucleotide of claim 79, wherein the rRNA is the 28S rRNA.

81. (Withdrawn) The oligonucleotide of claim 78, wherein the rRNA is prokaryotic.

82. (Withdrawn) The oligonucleotide of claim 81, wherein the rRNA is the 23S rRNA.

83. (previously presented) A method for depleting or isolating a targeted rRNA from a sample comprising:

a) obtaining a kit comprising: a capture oligonucleotide comprising a capture region and a magnetic bead; and at least a first bridging oligonucleotide comprising (1) at least one bridging region complementary to all or part of the capture region of the capture oligonucleotide and a (2) at least one targeting region comprising 10 contiguous nucleic acids complementary to a sequence of an rRNA;

b) incubating the sample with the bridging oligonucleotide under conditions allowing hybridization between the targeting region and the targeted rRNA;

c) incubating the bridging oligonucleotide with the capture oligonucleotide under conditions allowing hybridization between the bridging region and the capture region; and

d) isolating the targeted rRNA from the remainder of the sample by incubating the sample with a magnetic field.

84. (Original) The method of claim 83, further comprising:

e) obtaining the remainder of the sample enriched for mRNA;

f) preparing cDNA from the mRNA.

85. (Original) The method of claim 84, further comprising:

g) constructing a nucleic acid array with the cDNA.

86. (new) The method of claim 1, wherein the targeted nucleic acid is depleted by at least 50% in the sample.

87. (new) The method of claim 86, wherein the targeted nucleic acid is depleted by at least 60% in the sample.

88. (new) The method of claim 87, wherein the targeted nucleic acid is depleted by at least 70% in the sample.

89. (new) The method of claim 1, wherein the targeted nucleic acid is depleted by at least 80% in the sample.

90. (new) The method of claim 1, further comprising isolating the nontargeted nucleic acid in the depleted sample.